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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,089	10/16/2000	Hans J. Hansen	18733/1002	2717

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EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/688,089	HANSEN, HANS J.	
	Examiner	Art Unit	
	Sheela J Huff	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48,49,51-53,55,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48,49,51-53 and 55* is/are rejected.

7)☒ Claim(s) *58 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 9/3/04 has been considered and is persuasive-in-part. Claims 48-49, 51-53 and 55 and 58-59 are pending.

The rejection of claims 58 and 59 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's evidence of public availability. However, they were publically available as of 2/22/99 (MN-14) and 11/17/98 (WI2) therefore applicants priorty date for claims 58 and 59 is 10/16/00. Additionally, in view of the declarations filed 12/03 it is clear that MN-14 and WI2 were not publically available prior to the aforementioned dates.

The rejection under 35 USC 103 has been re-formulated to include a textbook definition in place of applicant's admission.

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 48-49, 51-53 and 55 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al PNAS vol. 90 p. 720 (1/1993), WO 92/15322, Wagner et al, Biotechnology Therapeutics vol. 3 p. 81 (1992) and Riott et al IMMUNOLOGY, 3rd Edition, pages 7.8-7.14 (Mosby, 1993) and further in view of Hansen et al, Cancer vol. 71 p. 3478 (1993).

Eshhar et al disclose the construction and use of chimeric genes comprised of a single-chain Fv domain of an antibody linked to the T cell receptor (TCR) or CD3, which is the principal triggering receptor complex of T cells(p. 720-second column-second full paragraph). The mechanism of action of the gene, includes being expressed in T cells, and when encountering the antigen, the complex emits signals for T cell activation, which results in the secretion of lymphokines and target cell lysis. (p. 720-second column-top). This reference also discloses the use of such chimeric genes in adoptive immunotherapy(p. 720-first column, first paragraph after the abstract).

The only difference between the instant invention and the reference is a specific showing that the chimeric gene can use used in adoptive immunotherapy, a specific showing that the immunoglobulin used can recognize a TAA or a disease caused by an infectious agent and the use of cytokines and/or the administration of an anti-ID and the specific use of CEA.

The WO shows that such chimeric genes can be used in adoptive immunotherapies where the disease is either a tumor or an infectious state(p. 29 and p. 1).

Roitt et al discloses that cytokines are known in the art to enhance the immune system. See Figure 7.14, which shows that IFN-gamma is involved in immunoregulation, B cells differentation and that IL-2 is involved in proliferation and activation. On page 7.9, the reference further discloses that IFNgamma activated macrophages and their capacity to act as APCs and that excess production of IFNgamma can play a part in the induction of autoimmunity. Furthermore, in Fig. 7.18, the reference states IL-2 is essential in "promoting T cell division and the release of mediators such as" IFN gamma and that IL-2 also potentiates B cell growth and "the activation of monocytes and natural killer cells in important in amplifying the immune response." Thus, the reference is saying that these cytokines are involved in the activation of the immune system. This is also evidenced by applicant's specification, page 22, lines 10-24.

Wagner et al teach the approach of tumor immunotherapy by the activation of the idiotypic network. This approach uses both Ab1 and Ab2 antiboides and produce an Ab2β which mimics the TAA. Thus, this reference not only shows that antibodies directed against TAA are know but also that the induction of the idiotypic network results in tumor therapy. See entire reference.

Hansen et al shows that CEA is a TAA (see entire reference). CEA is a well known tumor associated antigen that is expressed most adenocarcinomas of entodermally-derived digestive system epithelia, breast tumor cells and non-small cell lung cancer cells (see pages 1-2 of specification).

In view of the disclosure in Eshhar et al to use the chimeric genes in adoptive immunotherapy and in view of the disclosure of the WO which shows that such chimeric genes can be used in diseases caused by either tumors or infectious agents, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the chimeric genes of Eshhar et al in adoptive immunotherapy to treat tumors and infectious diseases. In view of the additional disclosure of Eshhar et al that many adoptive immunotherapy techniques lack specificity, it also would have been obvious to have the immunoglobulin encoding region of the chimeric gene encode an antibody that was specific for specific antigens on the surface of cells (ie TAA's). As demonstrated in Wagner et al, such antibodies are known in the art. Since it is within the purview of one skilled in the art two combine two known treatment techniques, it also would have been obvious to induce the idiotypic network (as described by Wagner et al) in combination with adoptive immunotherapy technique of Eshhar et al. In view of the well known knowledge that CEA is well known TAA, the use of CEA in the adoptive immunotherapy would have also been obvious to one or ordinary skill in the art.

Response to Applicant's arguments

Applicant argues that there is confusion in the art as to Class III anti-CEA antibodies and that the examiner did not consider all the references cited in the previous response. As disclosed by Hansen et al they clearly define a class III anti-CEA antibody (NP4) and they clearly differentiate it between class II and class I anti-CEA antibodies. The other references do not mention NP4 nor do they dispute the fact that NP4 is a

class III anti-CEA antibody. The examiner is not ignoring these other references, the other reference clearly do not cast any doubt on the classification of the class III anti-CEA antibody (NP4).

Applicant argues that the reference do not teach the addition of cytokines. In applicant's admission they refer to Riott et al (a general textbook) which clearly shows that IL-2 and IFNgamma are involved in activation of the immune system. Thus, in view of textbook, the additional use of cytokines is obvious to one of ordinary skill in the art.

Allowable Subject Matter

Claims 58 and 59 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Mondays and Thursdays from 5:30am to 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh